

basic Fibroblast Growth Factor

=Abstract=

Serum and Urine Basic Fibroblast Growth Factor (bFGF) in Cervical Cancer Patients

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Objectives: Angiogenesis takes place during both physiological and pathological processes, such as tumor development. Basic FGF is one of angiogenic factors. We investigated the serum and urine bFGF levels in patients with cervical cancer in contrast to those of normal control group to assess whether the serum and urine bFGF levels are useful markers to predict therapeutic effects of the patients with cervical cancer.

Methods: We measured serum and urine bFGF concentrations by ELISA in 28 patients with cervical cancer, as well as 25 normal volunteers and 38 patients with cervical intraepithelial neoplasia. Especially in 22 patients with cervical cancer, we measured serum bFGF levels before and after radiotherapy or radical hysterectomy with neoadjuvant chemotherapy.

Results: There were statistical differences among the serum bFGF levels in patients with cervical cancer (28.6 ± 30.4 pg/ml), cervical intraepithelial neoplasia (8.8 ± 11.3 pg/ml), and normal control group (5.2 ± 6.2 pg/ml) ($p < 0.05$). Patients undergoing cancer therapy had lower values than those without cancer therapy ($p < 0.05$).

Conclusion: Serum bFGF may help in diagnosing and predicting the therapeutic effects of the patients with cervical cancer. So we suggest that serum bFGF may be useful as a diagnostic and prognostic factor in cervical cancers.

Keywords: Serum bFGF, Urine bFGF, Cervical cancer, Angiogenesis

.1)

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.2)

가

가

3) bFGF가

(angiogenesis) .4) ,

가

18) In vitro bFGF가

가

19) , 20) , 21) bFGF

,22) ,23) 24)

bFGF

.56) 20 가 , 가

basic fibroblast growth factor(bFGF), acidic fibroblast growth factor(aFGF), vascular endothelial growth factor(VEGF), transforming growth factor (TGF-), tumor necrosis factor (TNF-), platelet derved endothelial growth factor(PDGF), pleiotrophin (PTN) .7)

가

.8) bFGF

가

.9) VEGF KDR

가

.10)

1. 1995 9 1997 6

FGF 9

bFGF가 가 .11) bFGF 25

16 18 kDa

12) 38

130 kDa bFGF

.13-14)

, , ,

.15) 28 5 cc

bFGF - 20

bFGF 22

.16) heparinase

heparan sulfate bFGF가 2.

.17) 1) bFGF

heparan normal mouse

sulfate 가 가 bFGF serum 가 10%

plate well 1 × (Wash Buffer) 200
 μ L 37 (incubation)
 well 7
 bFGF standards(0 80 fm/ml) 100 μ L 7
 plastic wrap 37 3 incubation
 well 300
 μ L 5 well bFGF
 Monoclonal antibody(R & D, Minneapolis, U.S.A) 100
 μ L 7 plastic wrap 1
 . 50 × Working Conjugate
 well 100 μ L plastic wrap
 30
 Working Substrate well 100
 μ L , 1
 Stop solution 100 μ L 7 (spe-
 ctrophotometer, Pharmacia, Head Office, Uppsala, Swi-
 den) 490 nm optical density(O.D.) ,
 2) bFGF
 1 ml
 creatinine 20 ml 4
 8 3000 rpm . super-
 natant 1.2 μ m pole size
 4 24
 6000 8000
 2 lyophilization 100 μ L
 25% bovine milk protein, 100 g/ml
 heparin, 10 g/ml mouse immunoglobulin G
 PBS 1% 7
 bFGF enzyme
 immunoassay
 hydration 7
 bFGF
 7.3
 b

bFGF(bFGF/g creatinine) = $\frac{\text{urine level of bFGF(pg/L)}}{\text{urine level of creatinine(g/L)}}$

3)

bFGF bFGF

Anova with multiple comparison

bFGF Wilcoxon signed rank test

1. bFGF
 bFGF 28.6 ± 30.4
 pg/ml
 bFGF 7 (p
 < 0.05) 8.8 ± 11.3
 pg/ml
 (Table 1, p > 0.05).

2. bFGF
 bFGF 275.8 ± 234.2
 pg/g 216.6 ±
 162.1 pg/g 184.1 ± 139.8 pg/g
 (Table 1).

3. bFGF
 11 45.5 ±
 b

Table 1. Serum bFGF levels of each groups

	Case(n)	serum bFGF(Mean ± S.D.)	urine bFGF(Mean ± S.D.)
Normal	21	5.2 ± 6.2 pg/ml*	184.1 ± 139.8 pg/g
CIN	38	8.8 ± 11.3 pg/ml	216.6 ± 162.1 pg/g
Cervical cancer	28	28.6 ± 30.4 pg/ml*	275.8 ± 234.2 pg/g

*p < 0.05 Anova with multiple comparison

CIN=cervical intraepithelial neoplasia

		SCCA \uparrow
	23.5 \pm 28.7 pg/ml	12.4 \pm 10.8
pg/ml		(Table 2, p < 0.05,
Fig. 2) CEA	31.0 \pm 8.9 pg/ml	29.9 \pm 11.8 pg/ml
bFGF		33.1 \pm 32.5
pg/ml	18.6 \pm 11.8 pg/ml	
		(Table 2, p <
0.05, Fig. 3).		

Table 2. Comparison of serum bFGF levels according to management and clinicopathologic characteristics in cervical cancer patients

	Case (n=22)
Age	45.5 \pm 7.3
Stage	
b	14
a	8
Tumor	
< 4 cm3	10
> 4 cm3	12
Histology	
Keratinizing, large cell	8
Nonkeratinizing, large cell	10
Small cell	4
Tx	
Radiotherapy	18
Operation with adjuvant chemotherapy	4
Before treatment (mean \pm S.D.)	
Serum bFGF	33.1 \pm 32.5 pg/ml
SCCA	23.5 \pm 28.7 pg/ml*
CEA	31.0 \pm 8.9 pg/ml
After treatment(mean \pm S.D.)	
Serum bFGF	18.6 \pm 11.8 pg/ml
SCCA	12.4 \pm 10.8 pg/ml*
CEA	29.9 \pm 11.8 pg/ml

*p < 0.05 Wilcoxon signed rank test

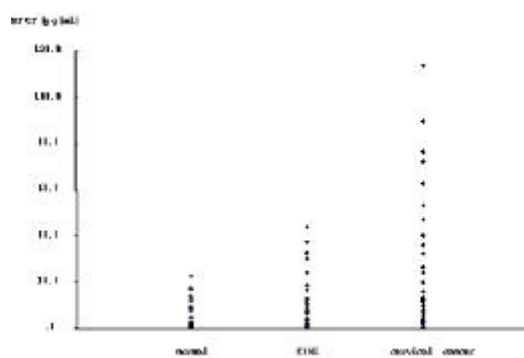


Fig. 1. The circulating levels of serum bFGF in normal controls, patients with CIN and cervical cancer. The cut off level of serum bFGF concentrations was decided to be 17.6 pg/ml, which was calculated as the mean+2SD of normal controls (not shown).

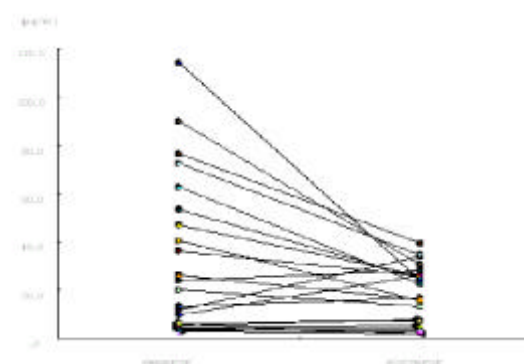


Fig. 2. Decrease in the circulating levels of serum SCCA after therapy in cervical cancer patients.

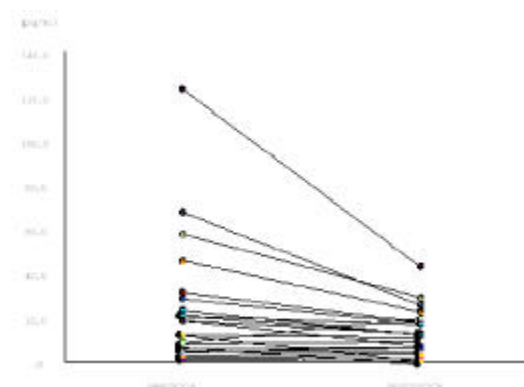


Fig. 3. Decrease in the circulating levels of serum bFGF after therapy in cervical cancer patients.

가 bFGF urokinase type plasminogen activator 가

.29) collagen,

.30) laminin, integrin 가

FGF .38)

.11,13)

FGF acidic FGF(FGF1), basic FGF(FGF2), FGF3 4(hst, int2), FGF5, FGF6, FGF7(), FGF8(가 .29) mm FGF 14가 가 . FGF 2 cm 가 .5) FGF heparin tyrosine kinase FGF .17) .8,10) bFGF 146 , 가 가 .31) bFGF .32) 가 가 .37) , , 가 .8,39,40,41) .33) bFGF bFGF , , bFGF가 .9,18) bFGF가 ,19) .20) 21) 22) , .24) .41) Kaposi 23) .34,35) bFGF heparinase heparan sulfate 가 가 .9) 17) bFGF heparane bFGF mRNA .19) sulfate .18) bFGF .36) 가 .19,21,23) bFGF mRNA 56) 가 가 bFGF 가 . bFGF bFGF가 .16) CA-153, CEA가 .37) bFGF

12.4 ± 10.8 pg/ml, 18.6 ± 11.8 pg/ml

bFGF .26)

bFGF bFGF Sliutz 47) bFGF가 bFGF

.27) bFGF가 bFGF가 10 bFGF

가 가 , 가 9.57 pg/ml

가 .42) bFGF bFGF가 가 bFGF

.27) bFGF가 가 bFGF

bFGF가 가 bFGF가

bFGF 가 .2542) bFGF

bFGF bFGF 가 가 bFGF .48) bFGF

.33) bFGF .4344) bFGF가 bFGF

bFGF .45) bFGF .27)

, bFGF 5.2 ± 6.2 pg/ml, 8.8 ± 11.3 pg/ml, 28.6 ± 30.4 pg/ml

bFGF가 가 bFGF가 가 bFGF

bFGF bFGF mRNA 가 bFGF

bFGF bFGF가 가 bFGF가 가

.46) bFGF .42)

bFGF가 가 , bFGF 184.1 ± 139.8

SCCA pg/ml, 216.6 ± 162.1 pg/ml, 275.8 ± 234.2 pg/ml

bFGF bFGF

SCCA CEA bFGF가 bFGF

bFGF SCCA bFGF가 bFGF

23.5 ± 28.7 pg/ml, 33.1 ± 32.5 pg/ml

가

가

SCCA가

bFGF가

bFGF

가

가 가

28

bFGF

가

b

22

bFGF가

가

SCCA가

bFGF

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